UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,294	03/22/2004	Scott R. Presnell	99-106C1	2898

10117 7590 09/20/2007

ZYMOGENETICS, INC.
INTELLECTUAL PROPERTY DEPARTMENT
1201 EASTLAKE AVENUE EAST
SEATTLE, WA 98102-3702

EXAMINER	
O HARA, EILEEN B	
ART UNIT	**PAPER NUMBER**
1646	

MAIL DATE	DELIVERY MODE
09/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/806,294	PRESNELL ET AL.	
	Examiner	Art Unit	
	Eileen B. O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-14 are pending in the instant application. Claims 11, 12 and 14 have been amended as requested by Applicant in the Paper filed February 7, 2007.

Election/Restrictions

2. Applicant's election of the species of inflammatory diseases related to arthritis in the reply filed on 2/7/07 is acknowledged.

Priority

3. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). In the first sentence of the specification, that status of parent 09/746,375 should be updated. See 37 CFR 1.78 and MPEP § 201.11.

Specification

4. The disclosure is objected to because of the following informalities.

4.1 On page 17, lines 4 and 12, "#######" should be replace with a PCT application number.

4.2 The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see pages 79, 93 and 117). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-14 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial utility or a well established utility.

Claims 1-14 are directed to methods for detecting a genetic abnormality, cancer or inflammation in a patient (or method of detecting activated T-cells in a patient suffering from inflammation), respectively, comprising hybridizing a polynucleotide which may or may not be labeled comprising nucleotides 123-557, 57-557, 21-557 of SEQ ID NO: 1 or the complements thereof with a genetic, tissue or biological sample from the patient, and comparing either the first reaction product to control reaction product from a wild type patient or from a normal control or biological sample, or comparing the degree of hybridization of the first reaction product from the tissue or biological sample with that of a control from a wild type patient, or comparing the level of labeled polynucleotide hybridization from the first reaction product from the tissue or biological sample with that from a normal control tissue or biological sample, wherein a difference in the reaction product or degree of hybridization or difference in level in the labeled polynucleotide hybridization, or in the case of detecting activated T-cells, an increase in the labeled polynucleotide hybridization in sample relative to control, indicates a genetic abnormality, cancer or inflammation. However, the claimed methods do not have any specific and substantial utility, or a well established utility, as determined according to the current Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001.

The instant specification teaches that the nucleic acid molecule of SEQ ID NO: 1 encodes a protein designated ZCYTO18, which is presumably a cytokine based on cellular expression and structure (four-helical-bundle structure). The specification further teaches that ZCYTO18 was isolated from tissue known to have important immunological function and which contain cells which play a role in the immune system, (is expressed in CD3+ selected, activated periperal blood cells), that this suggests that ZCYTO18 expression may be regulated and increase after T cell activation, and may have an effect on the growth/expansion and/or differentiated state of T- or B-cells, T- or B-cell progenitors, NK cells or NK progenitors. On pages 68-69, and 102-103, the specification discloses that mice injected with ZCYTO18 adenovirus display weight-loss, loss of mobility and a failure to groom, and a reduction in circulating lymphocytes, which are changes typical of those seen during septic shock and other inflammatory conditions. Also seen is a reduction of platelets. Page 78 of the specification teaches that ZCYTO18 is located at the 12q15 region of chromosome 12, near 12q14, where another T-cell expressed cytokine, interferon-gamma, maps, and that several genes map to the ZCYTO18 locus that are associated with human disease states, such as cancer. The 12q13-q15 region is involved in a variety of malignant and benign solid tumors, with 12q15 as a common break point. Because there is evidence for cancer resulting from mutations in the 12q15 region, the specification asserts that ZCYTO18 may be directly involved in or associated cancers. Page 79 of the specification also teaches other diseases and genetic abnormalities associated with this chromosomal region, and data on pages 103-104 indicate that ZCYTO18 may have an inhibitory activity on the proliferation/and or growth of a promyelocytic tumor cell line. Based on these factors, the instant application asserts that nucleic acids encoding ZCYTO18 can be used in methods to diagnose a

genetic abnormality, cancer or inflammation. However, ZCYTO18 has not been shown to be involved in any genetic abnormality, cancer or inflammation. There are no genetic mutations taught in ZCYTO18 that would correlate with any genetic abnormality leading to any disease state or disorder, and there is no information presented in the instant specification that an increase or decrease in expression of ZCYTO18 is correlated with any type of cancer or inflammation. There is no nexus between any genetic abnormality, cancer or inflammation and the molecules of the instant invention, so that these methods do not have a specific and substantial utility. A stated belief that a correlation exists between the nucleic acids and the above diseases or disorders, based on the limited information in the specification, is not sufficient guidance to use the claimed polynucleotides in the methods of detection; it merely defines a starting point for further research and experimentation. There is no RFLP polymorphism disclosed for this gene, or any other type of alteration that would result in a change in structure or expression, so the use of the ZCYTO18 nucleic acids as a diagnostic or prognostic marker is conjectural and would not, on the basis of the disclosure, be considered useful by one of skill in the art.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids. Significant further research would be required to determine even if the ZCYTO18 nucleic acids could be used in the methods of diagnosis or detecting. This further characterization, however, is part of the act of invention and until it has been undertaken the Applicant's claimed invention is incomplete.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-14 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Effective Priority Date

7. The effective priority date of the instant application has been determined to be Dec. 23, 1999, because provision application 60/172,105 teaches the nucleic acid molecule of SEQ ID NO: 1, and that the nucleic acid molecule can be used to detect genetic abnormalities, diagnose cancers, inflammation and detect CD3+ cells.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 are rejected under 35 U.S.C. 103(a) as obvious over Gurney et al., U.S. Patent No. 6,551,799, effective priority date Dec. 7, 1999 (60/169,495), in view of Lok et al., U.S. Patent No. 6,013,503, filing date May 1, 1988.

8. Claims 1-3 are drawn to detecting a genetic abnormality on chromosome 12q15 in a patient, comprising obtaining a genetic sample from a patient, producing a first reaction product by incubating the genetic sample with a polynucleotide, wherein the polynucleotide comprises a polynucleotide selected from the group consisting of a polynucleotide of nucleotides 123-557, 57-557 or 21-557 of SEQ ID NO: 1 or the complements thereof, wherein the incubation is under conditions wherein said polynucleotide will hybridize to a complementary polynucleotide sequence in the genetic sample, visualizing the first reaction product, and comparing the first reaction product to control reaction product from a wild type patient, wherein a difference between said first reaction product and said control reaction product is indicative of a genetic

abnormality on chromosome 12q15 in the patient, and wherein the genetic abnormality further comprises a gross chromosomal abnormality, a translocation, aneuploidy large insertion, large deletion, chromosome rearrangement, or a chromosome break at chromosome 12q15.

The '799 patent discloses a nucleic acid of SEQ ID NO: 1, which is 99.8% identical to the nucleic acid of SEQ ID NO: 1 and is 100% identical to the coding region of the nucleic acid of SEQ ID NO: 1 of the present application (nucleotides 21-557, see attached sequence alignment), and which encodes a protein identified as IL-22.

The '799 patent teaches:

(8) Interleukin-22 (IL-22) is a newly identified cytokine produced by activated T cells and is related to interleukin-10 (IL-10). IL-22 signals through a receptor complex comprised of CRF2-4, also known as IL-10R.beta., and a new member of the class II cytokine receptor family, interleukin-22 receptor (IL-22R) [Xie et al., J. Biol. Chem. (2000) 275, 31335-31339]. Of the members of this receptor complex, IL-10R.beta. is expressed in several tissues while the expression of IL-22R is fairly restricted, with high expression in the pancreas, suggesting that IL-22R is controlling the site of action of IL-22. As an example, murine IL-22 induces changes in gene expression in pancreatic acinar cells of several genes including pancreatitis associated protein (PAP1), a gene overexpressed in acute pancreatitis [Iovanna et al, J. Biol. Chem. (1991) 266, 24664-246691. IL-22 signaling through a receptor complex that is highly expressed in pancreas, suggests that IL-22 may modulate an immune/inflammatory response in the pancreas, and may be involved in diseases of the pancreas including pancreatitis.

(128) Nucleotide sequences encoding an IL-22 can also be used to construct hybridization probes for mapping the gene which encodes that IL-22 and for the genetic analysis of individuals with genetic disorders. The nucleotide sequences provided herein may be mapped to a chromosome and specific regions of a chromosome using known techniques, such as in situ hybridization, linkage analysis against known chromosomal markers, and hybridization screening with libraries.

The '799 patent does not teach the specific limitations in the method steps, or that the detectable chromosomal aberrations could include but are not limited to aneuploidy, gene copy

number changes, insertions, deletions, translocations, restriction site changes and

rearrangements.

Lok et al teach:

(85) The present invention also provides reagents for use in diagnostic applications. For example, the human PC4 gene, a probe comprising human PC4 DNA or RNA, or a subsequence thereof can be used to determine if the human PC4 gene is present on chromosome 19 or if a mutation has occurred. Detectable chromosomal aberrations at the human PC4 gene locus include, but are not limited to, aneuploidy, gene copy number changes, insertions, deletions, restriction site changes and rearrangements. These aberrations can occur within the coding sequence, within introns, or within flanking sequences, including upstream promoter and regulatory regions, and may be manifested as physical alterations within a coding sequence or changes in gene expression level. Analytical probes will generally be at least 20 nucleotides in length, although somewhat shorter probes (14-17 nucleotides) can be used. PCR primers are at least 5 nucleotides in length, preferably 15 or more nt, more preferably 20-30 nt. Short polynucleotides can be used when a small region of the gene is targeted for analysis. For gross analysis of genes, a polynucleotide probe may comprise an entire exon or more. Probes will generally comprise a polynucleotide linked to a signal-generating moiety such as a radio-labeled nucleotide. In general, these diagnostic methods comprise the steps of (a) obtaining a genetic sample from a patient; (b) incubating the genetic sample with a polynucleotide probe or primer as disclosed above, under conditions wherein the polynucleotide will hybridize to complementary polynucleotide sequence, to produce a first reaction product; and (iii) comparing the first reaction product to a control reaction product. A difference between the first reaction product and the control reaction product is indicative of a genetic abnormality in the patient. Genetic samples for use within the present invention include genomic DNA, cDNA, and RNA. The polynucleotide probe or primer can be RNA or DNA, and will comprise a portion of SEQ ID NO:1, the complement of SEQ ID NO:1, or an RNA equivalent thereof. Suitable assay methods in this regard include molecular genetic techniques known to those in the art, such as restriction fragment length polymorphism (RFLP) analysis, short tandem repeat (STR) analysis employing PCR techniques, ligation chain reaction (Barany, PCR Methods and Applications 1:5-16, 1991), ribonuclease protection assays, and other genetic linkage analysis techniques known in the art (Sambrook et al., ibid.; Ausubel et. al., ibid.; A. J. Marian, ibid., 1995). Ribonuclease protection assays (see, e.g., Ausubel et al., ibid., ch. 4) comprise the hybridization of an RNA probe to a patient RNA sample, after which the reaction product (RNA--RNA hybrid) is exposed to RNase. Hybridized regions of the RNA are protected from digestion. Within PCR assays, a patient genetic sample is incubated with a pair of polynucleotide primers, and the region between the primers is amplified and recovered. Changes in size or amount of recovered product are indicative of mutations in the patient. Another PCR-based technique that can be employed is single strand conformational polymorphism (SSCP) analysis (Hayashi, PCR Methods and Applications 1:34-38, 1991).

(196) The present invention also provides reagents which will find use in diagnostic applications. For example, the zsig63 gene, a probe comprising zsig63 DNA or RNA or a subsequence thereof can be used to determine if the zsig63 gene is present on chromosome 4 or if a mutation has occurred. Detectable chromosomal aberrations at the zsig63 gene locus include but are not limited to aneuploidy, gene copy number changes, insertions, deletions, translocations, restriction site changes and rearrangements. Such aberrations can be detected using polynucleotides of the present invention by employing molecular genetic techniques, such as restriction fragment length polymorphism (RFLP) analysis, short tandem repeat (STR) analysis employing PCR techniques, and other genetic linkage analysis techniques known in the art (Sambrook et al., ibid.; Ausubel, et. al., ibid.; Marian, A. J., Chest, 108: 255-20 265, 1995). These methods can be employed to use zsig63 polynucleotides to detect abnormalities on human chromosome 4, such as those described below.

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use the nucleic acid molecule of the '799 patent, and the method steps of Lok et al., to detect a genetic abnormality in the ZCYTO18 gene, since the '799 patent teaches that the encoded protein is IL-22, which is a cytokine that is involved in inflammation, and that nucleic acids encoding the protein can be used for the genetic analysis of individuals with genetic disorders. The method steps to perform this are standard in the art as shown by Lok et al., as are the type of chromosomal abnormalities that would be detected. The skilled artisan would be motivated to detect genetic abnormalities in the gene since the '799 patent teaches to do so, and there would be a reasonable expectation of success, since the method steps are well known and have been used widely and successfully used in the field of molecular biology. Although the '799 patent does not teach specifically that the chromosome is 12q15, the method of detecting an abnormality would by necessity occur at chromosome 12q15. Therefore, the invention is *prima facie* obvious over the references.

Conclusion

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (571) 272-0878. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nichol can be reached at (571) 272-0835.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://portal.uspto.gov/external/portal/pair. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Eileen B. O'Hara, Ph.D.

Patent Examiner

Eileen B. O'Hara

EILEEN B. O'HARA
PRIMARY EXAMINER